REMARKS

Claims 1-7 are pending in the instant application. Claims 1-3 and 5-7 have been amended. Claim 4 has been cancelled. New claims 8-13 have been added.

The Examiner has rejected claim 4 under 35 U.S.C. § 101 on the grounds that it is directed to nonstatutory subject matter. Claim 4 has been cancelled, rendering this rejection moot.

The Examiner has rejected claims 1-3 and 5-7 under 35 U.S.C. § 112 as failing to particularly point out and distinctly claim the subject matter which is regarded as the invention. The Examiner alludes to several specific examples of informal or unclear language, and Applicants have for the most part amended the claims in accordance with the Examiner's suggestions. For example, the parentheses have been deleted from the claims.

The phrase "separately or together" has been removed from claim 1 and replaced by language which more clearly defines the invention, and Applicants would like to clarify this matter further. The claims in general have been amended to recite the option of simultaneous or sequential administration of the active ingredients. The active ingredients of the instant invention, i.e., formoterol, salts thereof and budesonide, can be given to a patient separately via a device that has multiple compartments, each compartment containing an active ingredient of the invention. According to this aspect of the invention, a first

compound can be administered to a patient, to be followed shortly thereafter by a dose of a second active compound. Thus, the compounds are administered separately but sequentially. "Separate" administration of compounds can be regarded as a previously known procedure. In such a procedure, a compound can be given to a patient and this initial dose is followed by another compound some time later, with elapsed time between administration. On the other hand, a dosage of compounds can be given simultaneously as a mixture. That is, the compounds can be "combined" in a device as a mixture, and they thus can be administered to a patient simultaneously. The word preparation as used in the instant application refers to the mixture or composition of the compounds.

In claim 3, the term "preparation" has been deleted and the concept of combination has been clarified.

The word "it" in claims 5-7 has been deleted and replaced with language more clearly defining the invention. Claim 7 has been amended to recite a single administration step.

With regard to the phrase "for combination therapy," Applicants have left the language in the claims and maintain that such language is not superfluous and does not render the claims indefinite. The claims as amended more clearly point the significance of this phrase and its meaning with regard to the instant invention.

The phrase "and/or" has been removed from the original claims and replaced with "or." New claims 8-13 have been added to indicate that one aspect of the invention is pharmaceutical compositions, and methods for their use, which comprise formoterol and pharmaceutically acceptable salts or solvates thereof.

The Examiner also rejected claims 1-3 and 5-7 under 35 U.S.C. § 103 as obvious over U.S. Patents No. 3,983,233 to Brattsand et al. ("Brattsand") and No. 3,494,974 to Murakami et al. ("Murakami") in view of the acknowledgements on page 3 of the instant specification, i.e., (Ann. Allergy, 1989, 63: 220-224; Lung, 1990, 168, 105-110). Specifically, the Examiner asserts that Brattsand, col. 10, lines 7-8 suggests the use of a class of steroids which includes budesonide for treatment of respiratory disorders including asthma. The Examiner cites Brattsand examples 9 and 10 as disclosing inhalation aerosols. The Examiner further alleges that Murakami highlights a class of β_2-adrenoreceptor agonists, of which formoterol is a member which are bronchial smooth muscle relaxants and can be used in aerosol inhalation compositions.

The Examiner contends that it would have been *prima facie* obvious to one of ordinary skill in the art to combine two or more ingredients which are known to serve the same purpose, since the idea to combine is the logical outcome of their

separate prior art use (In re Kerkhoven) especially in view of the combination of EP416950 and 416951 on page 3, lines 21, 22 and 25-32 of the instant application. Applicants respectfully disagree with the Examiner.

Applicants agree with the Examiner that the reference of Brattsand discloses a class of corticoid compounds which may be effective in the treatment of various inflammatory diseases. However, Brattsand does not disclose or claim the use of these compounds in composition with other active ingredients such as β_2-adrenoreceptor agonist for combination therapy which would have an additive and positive effect in the treatment of respiratory disorders, as is claimed in the instant application. In addition, the budesonide of the instant applicant is a pharmacologically very safe (pages 2-3 of specification) compound and has proven to be particularly highly effective in the long-term management of chronic inflammation associated with asthma.

The Applicants disagree with the Examiner that the reference of Murakami discloses the compound of the present invention for administration via the route of the instant invention. Murakami discloses compounds which are α-aminoethylbenzyl derivatives but not that which is the active ingredient according to the instant invention. Furthermore, Murakami discloses only prophetically that the compounds "may also be in the form of aerosols as inhalations" (paragraph

bridging col. 7 and 8), since the use of compound 3-formylamino-4-hydroxy-alpha-[N-91-methyl-2-p-methoxyphenylethyl)-aminoethyl)benzyl alcohol, Example 22 cited by the Examiner (col. 7, lines 35-47), was tested using intravenous injections. In addition, there are no claims or disclosure in Murakami of formulations to be used for the treatment of respiratory disorders. Murakami only discloses the method of synthesis of compound of Example 22.

Both European patent applications disclosed by the apllicants on page 3 of the specification relate to pharmaceutical compositions containing two active ingredients in combination. However, the combination of budesonide and formoterol is not mentioned in the cited European applications. The instant combination is novel and exhibits significantly enhanced and unexpected properties over the prior art combinations. Formoterol not only allows budesonide to exhibit its desired effect, but contributes to a synergistic effect consisting of enhanced patient compliance. The opinion in the art has been that such combinations as that disclosed in the instant application would not help most patients with asthma as such a combination would prevent the flexible use of the individual components. Therefore, one of ordinary skill in the art would not have been motivated to combine the active ingredients of the instant invention with the expectation of such high efficacy in the treatment of respiratory disorder.

Based on the above, it is submitted that the application is in condition for allowance. Reconsideration and allowance of amended claims 1-3 and 5-7 as well as allowance of new claims 8-13 are respectfully requested.

Any additional fees due in connection with this response should be charged to Deposit Account No. 23-1703.

Date: July 19, 1993

Respectfully submitted,

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Enclosure